

NOTICE OF REDUNDANCY

The hanging committee of *Sexually Transmitted Infections* wishes to announce that two published papers by van Valkengoed *et al.*² exhibit a degree of overlap. Specifically, the female patients are the same in both papers. They are indistinguishable from the point of population size (5714), age (15–40), setting, participation rate (51%), chlamydia prevalence rate (2.8%; CI 2.1–3.4%), and the number of women excluded because of never having been sexually active (125). There is also a certain degree of overlap between the two papers in the introduction, methods, results, and discussion sections.

- 1 Van Valkengoed IGM, Boeke JAP, Moore SA, *et al.* Disappointing performance of literature-derived selective screening criteria for asymptomatic Chlamydia trachomatis infection in an inner-city population. *Sex Transm Dis* 2000;27:504–7.
- 2 Van Valkengoed IGM, Morré SA, van den Brule AJC, *et al.* Low diagnostic accuracy of selective screening criteria for asymptomatic Chlamydia trachomatis infections in the general population. *Sex Transm Inf* 2000;76:375–80.

Reply

We strongly disagree with your conclusion that we are guilty of duplicate publication. The objectives, analyses, and results presented in the two papers in *Sexually Transmitted Diseases* (paper 1)¹ and *Sexually Transmitted Infections* (paper 2)² are completely different and do not resemble each other at all. The aim of paper 1 was to determine the value of currently publicised screening criteria for asymptomatic populations as selection criteria for the general population. A literature review was performed to identify criteria for women. Criteria for men were not available. These criteria were then applied to the female participants in the Amsterdam Screening Study. The diagnostic accuracy of these criteria was then found to be poor. That led to the second research question, which was addressed in paper 2: Could suitable new criteria for selective screening of females and males be derived from our own study population? In paper 2 we report on the development of this new set of selective screening criteria and their diagnostic accuracy. In addition, detailed prevalence data and the results for both men and women non-respondents in the Amsterdam Screening Study were presented.

The papers did not contain references to each other. This was not through intent, but because of the simultaneous process of submission for publication. At the time of submission, there was simply no other "paper" to refer to. When checking the proofs of the papers we should have added "in press" to the references, which we neglected to do. We sincerely apologise for this and will remember to do so in future.

In summary, we believe your verdict of duplicate publication to be unjust and your sanction to be too harsh for the omission of cross references.

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- 1 Van Valkengoed IGM, Boeke JAP, Morré SA, *et al.* Disappointing performance of literature-derived selective screening criteria for asymptomatic Chlamydia trachomatis infection in an inner-city population. *Sex Transm Dis* 2000;27:504–7.
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LETTERS TO THE EDITOR

Prevalence of Chlamydia trachomatis IgG antibodies in antenatal patients from Trinidad

EDITOR,—A recent study in Jamaica by Dowe *et al.* using cell culture and a direct fluorescence assay (DFA) showed a prevalence of *Chlamydia trachomatis* infection in 47% of gynaecological patients.¹ Unfortunately, there are no comparable data for cell culture and DFA in Trinidad. Moreover, we cannot find any reports on serological studies for *C. trachomatis* IgG antibody in the West Indies. In an attempt to shed more light on prevalence of *C. trachomatis* IgG antibody in pregnant women in Trinidad, we collected 56 serum specimens (mean age of patients 27 years) with ethics committee approval from one clinic at the general hospital, Port of Spain. As well as testing these sera by an in-house ELISA method based on that described by Ossewaarde *et al.*,² we also used a commercial ELISA test specific for *C. trachomatis* IgG (Savyon Diagnostics, Israel) and the whole inclusion immunofluorescence (WHIF) test as previously described by Richmond and Caul.³

All collected sera were stored at -70°C until analysis. Samples were subsequently coded and tested blind in duplicate in laboratories in Sheffield and Bristol. Details of the in-house ELISA test methodology and interpretation of readings using microimmunofluorescence (MIF) serum positive and negative controls were described in Keay *et al.*⁴ The commercial ELISA was performed according to the manufacturer's instructions. The WHIF test consisted of chlamydial inclusions of infected mammalian cells with LGV2 mounted on a glass well or coverslip. The WHIF titre is described as the highest dilution of antibody where the inclusion can be clearly seen by fluorescence staining.

For the ELISA tests, results were recorded as positive, negative, or equivocal. For the WHIF test, titres between 1:64 and 1:256 were recorded as such; a low titre was $\leq 1:64$ and a high titre $\geq 1:512$.

Twenty five (45%) and 29 (52%) samples were positive for the commercial and in-house ELISA tests respectively. Eighteen (32%) samples had a titre of ≥ 512 in the WHIF test, as shown in table 1.

The latter finding is of note. It is accepted that *C. trachomatis* is an established pelvic

Table 1 Comparison of ELISA and WHIF tests showing the Chlamydia trachomatis IgG antibody titre distribution

| WHIF test | Commercial ELISA | | | In-house ELISA | | |
|------------|------------------|----|---|----------------|----|---|
| | + | Eq | – | + | Eq | – |
| ≥ 512 | 15 | 1 | 2 | 18 | – | – |
| 256 | 3 | – | 1 | 3 | 1 | – |
| 128 | 4 | – | – | 2 | 1 | 1 |
| 64 | 2 | – | 4 | 4 | 1 | 1 |
| ≤ 64 | 1 | 1 | 1 | 2 | – | 1 |

Eq = equivocal.

pathogen and in a recent study of 34 women positive for *C. trachomatis* IgG ($\geq 1:128$) by ELISA, at laparoscopy 31 (91.2%) were diagnosed as having tubal disease.⁵ It is likely that significant damage could be occurring in these patients as a previous study looking at high *C. trachomatis* IgG titres showed 46% positive and 8% positive in infertile women with damaged and normal tubes, respectively.⁶

Although these findings are based on relatively small numbers, they are of significant concern if combined with the other most recent study.¹ It would appear that the prevalence rates for *C. trachomatis* may well be high and that data presented here suggest possible future PID development and resultant sequelae. It is clear that further studies are warranted and that screening and treatment strategies may be required urgently to curtail considerable morbidity in Trinidad and throughout the West Indies in general.

- High prevalence of *C. trachomatis* IgG antibodies in antenatal patients in Trinidad
- Prevalence rates of *C. trachomatis* in Trinidad are similar to those from Jamaica
- Good correlation of in-house and commercial ELISA tests with WHIF test
- Urgent need for screening and treatment strategies for *C. trachomatis* in West Indies

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Implications of random measurement error in studies adjusting for sexual behaviours

EDITOR,—In their recent review of methodological issues in sexual behaviour research, Fenton *et al.*¹ provide a comprehensive overview of the major types of sexual behaviour research, the sources of measurement error which may affect such research, and different approaches to measuring various forms of measurement error. We would like to provide an important footnote on the implications of the poor measurement of sexual behaviours for drawing inferences from studies of sexually transmitted infections (STIs) which attempt to adjust for sexual behaviours in their analyses.

The role of systematic measurement errors in study design and analysis, as described by Fenton *et al.*, is widely recognised. Given their impact on inferences of association, great care is taken in most studies to avoid these biases. The effects of random measurement error, or non-differential misclassification, on epidemiological inference typically receive less attention. Most researchers realise that non-differential misclassification of exposure and/or outcome measures will lead to an attenuation of the resulting measure of association.

However, the fact that random measurement error in potential confounding variables may wreak havoc on the inferences which are made from study results is seldom acknowledged. The non-differential misclassification of a dichotomous confounding variable may lead to inadequate statistical adjustment (often referred to as residual confounding) and the false appearance of statistical interaction when none is present.² When confounders are measured as polytomous or continuous variables (for example, condom use never/sometimes/always or number of sexual partners), random measurement error can bias the adjusted measure of association unpredictably—in some instances making the adjusted measure of association less accurate than the crude.^{3–5} These forms of misclassification are generally of greatest concern when the true exposure-disease association is relatively weak compared with the exposure-confounder and outcome-confounder relation,⁵ as is the case in most research around STIs. Even small random errors can have major effects on adjusted measures of association, and the unpredictability of the effects of misclassification may be compounded in multivariate analyses.⁶

With this in mind, Fenton *et al.*'s review of the difficulties involved in the accurate measurement of sexual behaviour has powerful implications for studies attempting to control for covariates associated with risk for STIs. Studies which attempt to adjust during statistical analysis for numbers and types of sexual partners, frequency of sexual contacts, or condom use practices, are likely to

encounter some degree of random measurement error. Although perhaps non-differential with respect to exposure or outcome, this mismeasurement may lead to unpredictable biases and/or mis-specified analyses, and in turn, spurious inferences.

In summary, the inadequate measurement of sexual behaviour requires special consideration in any study attempting to adjust for the confounding role of sexual behaviours in associations involving STIs. We hope that Fenton *et al.*'s review of the challenges posed by the collection of sexual behaviour data helps to draw attention to this frequently overlooked methodological aspect of the epidemiology of STIs.

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Is *Mycoplasma hominis* a vaginal pathogen?

EDITOR,—We would like to comment on the study by Arya and colleagues¹ in which they failed to find evidence for *Mycoplasma hominis* being pathogenic in the vagina, or otherwise contributing to bacterial vaginosis (BV). They mentioned the 21 year old review of Taylor-Robinson and McCormack² who surmised that *M. hominis* might act in symbiosis with other organisms or as a sole pathogen in BV. The latter was referred to as non-specific vaginitis or *Gardnerella* associated vaginitis at that time, the term BV being used from about 1984. Since then, much has been learned about the vaginal microflora in health and disease, but the question of which bacteria, if indeed any, cause BV remains unanswered. The few *M. hominis* organisms in the healthy vagina appear to behave as commensals. We challenged³ the suggestion of Mårdh and colleagues that *M. hominis* was associated with a number of genital signs and symptoms after BV had been excluded, our assertion being that *M. hominis* organisms outside the context of BV would be present in small numbers and, therefore, unlikely to cause a problem. In contrast, the few *M. hominis* organisms in the healthy vagina increase

in number, perhaps by 10 000-fold or more, in the vagina of women with BV. This increase, however, occurs only late in the development of BV.⁴ Indeed, it is rare to find large numbers in the “intermediate” (grade 2) stage between the normal vaginal flora and “full blown” BV (grade 3). Thus, in the study by Arya and colleagues we have difficulty in understanding why only 35 (48%) of the 73 women with *M. hominis* positive BV had large numbers of organisms ($>5 \times 10^5$). A Gram stain evaluation should have distinguished women with grade 2 flora from those with grade 3. Be this as it may, the authors contend that because the additional presence of *M. hominis* with *G. vaginalis* and strict anaerobes did not seem to increase the likelihood of the women developing BV, *M. hominis* is not involved. It is clear that *M. hominis* organisms are not essential for the development of BV and unlikely that their initial presence in the vagina increases the likelihood of BV developing. However, if they are present in the vagina initially, then they will multiply as indicated and large numbers will ensue. The data of Arya and colleagues do not resolve the issue of whether large numbers contribute to the disease process or are involved in its persistence. Against this, as they point out, is a study⁵ in which metronidazole, inactive *in vitro* against *M. hominis*, cleared vaginitis, and doxycycline, active against *M. hominis*, did not. However, it should also be remembered that *M. hominis* organisms caused pharyngitis and cervical lymphadenopathy when given orally in large numbers to volunteers,⁶ indicating the pathogenic potential of the organisms. Furthermore, the *M. hominis* species is heterogeneous, some strains having greater epithelial cell adherence properties than others. We do not see any data that point to *M. hominis* being a sole pathogen or co-pathogen in the vagina but, equally, we are not convinced by data that purport to show that it is not.

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Response of hepatitis B induced membranoproliferative glomerulonephritis to HAART

EDITOR,—Renal disease occurring in HIV infected individuals is well described.^{1,2} HIV associated nephropathy (HIVAN) is the